08/907,041

=> d his

(FILE 'HOME' ENTERED AT 19:24:47 ON 01 DEC 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 19:25:55 ON 01 DEC 2003

L1 148987 S GLUTAMYL(W)TRANSPEPTIDASE OR GLUTATHIONE(W)PEROXIDASE OR CATA
L2 148673 S METALLOTHIONASE OR SUPEROXIDE(W)DISMUTASE OR BLEOMYCIN(W)HYDR
L3 251264 S L1 OR L2
L4 2798 S L3(6A)(DNA OR POLYNUCLEOTIDE OR NUCLEIC(W)ACID)
L5 8679 S PROTECT?(10A)(TOXIC(W)SPECIES OR FREE(W)RADICAL OR SUPEROXIDE
L6 14 S L4 AND L5
L7 11 DUP REM L6 (3 DUPLICATES REMOVED)

=> d bib ab 1-11 l7

L7 ANSWER 1 OF 11 MEDLINE on STN DUPLICATE 1
AN 2002445359 MEDLINE
DN 22112975 PubMed ID: 12117500
TI Cloning, production and characterisation of a recombinant Cu/Zn superoxide dismutase from Taenia solium.
AU Castellanos-Gonzalez Alejandro; Jimenez Lucia; Landa Abraham
CS Departamento de Microbiologia y Parasitologia, Facultad de Medicina, Edificio A, 2do piso, Universidad Nacional Autonoma de Mexico, Ciudad Universitaria, Mexico D.F. 04510, Mexico.
SO INTERNATIONAL JOURNAL FOR PARASITOLOGY, (2002 Aug) 32 (9) 1175-82. Journal code: 0314024. ISSN: 0020-7519.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AF439353
EM 200211
ED Entered STN: 20020904
Last Updated on STN: 20021212
Entered Medline: 20021114
AB A full-length complementary **DNA** clone encoding a cytosolic Cu/Zn **superoxide dismutase** with a M(r) of 15,588 Da was isolated from a Taenia solium larvae complementary DNA library. Comparison analysis of its deduced amino acid sequence revealed a 71% identity with Schistosoma mansoni, 57.2-59.8% with mammalian and less than 54% with other helminth cytosolic Cu/Zn superoxide dismutase. The characteristic motifs and the amino acid residues involved in coordinating copper and zinc enzymatic function are conserved. The T. solium Cu/Zn superoxide dismutase was expressed in the pRSET vector. Enzymatic and filtration chromatographic analysis showed a recombinant enzyme with an activity of 2,941 U/mg protein and a native M(r) of 37 kDa. Inhibition assays using KCN, H(2)O(2), NaN(3) and SDS indicated that Cu/Zn is the metallic cofactor in the enzyme. Thiabendazole (500 microM) and albendazole (300 microM) completely inhibited the activity of T. solium Cu/Zn superoxide dismutase. Thiabendazole had no effect on bovine Cu/Zn superoxide dismutase; in contrast, albendazole had a moderate effect on it at same concentrations. Antibodies against T. solium Cu/Zn superoxide dismutase did not affect the enzymatic function; nevertheless, it cross reacts with several Taenia species, but not with trematodes, nematodes, pig, human and bovine Cu/Zn superoxide dismutase enzymes. Western blot analysis indicated the enzyme was expressed in all stages. These results indicate that T. solium possesses a Cu/Zn superoxide dismutase enzyme that can **protect** him from oxidant-damage caused by the **superoxide anion.**

L7 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:177838 CAPLUS

DN 136:290312
TI Melatonin reduces phosphine-induced lipid and DNA oxidation in vitro and in vivo in rat brain
AU Hsu, Ching-Hung; Chi, Bei-Ching; Casida, John E.
CS Department of Public Health, School of Medicine, Taipei Medical University, Taipei, Taiwan
SO Journal of Pineal Research (2002), 32(1), 53-58
CODEN: JPRSE9; ISSN: 0742-3098
PB Blackwell Munksgaard
DT Journal
LA English
AB Phosphine (PH3), a widely used pesticide, was found in our recent study to induce oxidative damage in the brain, liver and lung of rats. We also obsd. that melatonin significantly blocked this action. The present study focused on brain and the magnitude and mechanism of protection of PH3-induced oxidative damage by melatonin in vitro and in vivo. PH3 in whole brain homogenate (3 mg protein/mL Tris-HCl pH 7.4 buffer) induced increasing lipid peroxidn. [as malondialdehyde (MDA) and 4-hydroxyalkenals (4-HDA)] dependent on concn. (0.25-2 mM) and time (30-150 min), reaching a max. level of 2.9-fold at 90 min after PH3 at 1 mM. Elevation of MDA + 4-HDA levels by PH3 at 1 mM was also obsd. in homogenates of cerebral cortex, cerebellum, hippocampus and hypothalamus examd. individually. Melatonin at 0.1-2 mM progressively inhibited PH3-induced lipid peroxidn. in brain and regions thereof. Addnl., PH3 induced brain DNA oxidn. in vitro and in vivo detd. as 8-hydroxyguanosine (8-OH-dG). Melatonin at 1 mM significantly suppressed PH3-induced brain DNA oxidn. in vitro. PH3 at 4 mg/kg i.p. significantly elevated 8-OH-dG in frontal cortex and melatonin prevented it. PH3 in vivo marginally lowered brain glutathione peroxidase activity and melatonin restored it completely. In contrast, PH3 and melatonin both stimulated superoxide dismutase prodn. Brain glutathione (GSH) levels in PH3-treated rats were significantly reduced at 30 min and recovered gradually. It is concluded that melatonin, probably because of its **free radical** scavenging ability, confers marked **protection** against PH3-induced oxidative toxicity in brain.
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:910778 CAPLUS
DN 134:176857
TI Metallothionein inhibits peroxynitrite-induced DNA and lipoprotein damage
AU Cai, Lu; Klein, Jon B.; Kang, Y. James
CS Department of Medicine, University of Louisville, Louisville, KY, 40292, USA
SO Journal of Biological Chemistry (2000), 275(50), 38957-38960
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Previous studies have demonstrated that metallothionein functions as an antioxidant that **protects** against oxidative DNA, protein, and lipid damage induced by **superoxide anion**, hydrogen peroxide, hydroxyl radical, and nitric oxide. The present study was undertaken to test the hypothesis that metallothionein also protects from DNA and lipoprotein damage induced by peroxynitrite, an important reactive nitrogen species that causes a diversity of pathol. processes. A cell-free system was used. DNA damage was detected by the mobility of plasmid DNA in electrophoresis. Oxidn. of low d. lipoprotein was measured by a thiobarbituric acid-reactive substance, which was confirmed by lipid hydroperoxide assay. Plasmid DNA damage and low d. lipoprotein oxidn. were induced by 3-morpholinosydnomine, which produces peroxynitrite through the reaction between nitric oxide and superoxide anion or by synthesized peroxynitrite directly. DNA damage by 3-morpholinosydnomine

was prevented by both metallothionein and superoxide dismutase, whereas the damage caused by peroxynitrite was prevented by metallothionein only. The oxidn. of low d. lipoprotein by 3-morpholinosydnomine and peroxynitrite was also significantly inhibited by metallothionein. This study thus demonstrates that metallothionein may react directly with peroxynitrite to prevent DNA and lipoprotein damage induced by this pathol. reactive nitrogen species.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:617858 CAPLUS
DN 132:164494
TI Local hypomethylation in atherosclerosis found in rabbit ec-sod gene
AU Laukkanen, Mikko O.; Mannermaa, Sanna; Hiltunen, Mikko O.; Aittomaki, Saara; Airenne, Kari; Janne, Juhani; Yla-Herttuala, Seppo
CS A. I. Virtanen Institute, University of Kuopio, Kuopio, 70211, Finland
SO Arteriosclerosis, Thrombosis, and Vascular Biology (1999), 19(9), 2171-2178
CODEN: ATVBFA; ISSN: 1079-5642
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Extracellular superoxide dismutase (EC-SOD) **protects** arteries against deleterious effects of **superoxide anions** and the development of atherosclerosis. In this study, the authors cloned and characterized rabbit ec-sod gene. The authors identified 6 rabbit C-elements and 5 CpG clusters in the cloned sequence. One of the CpG clusters is located on the coding sequence. Because CpG clusters are potential sites for methylation and may explain the occurrence of mutations, methylation status of each of the CpG dimers located in the coding sequence CpG cluster was characterized using direct genomic sequencing. Unexpectedly, a marked redn. in the amt. of methylated CpG dinucleotides in ec-sod gene was detected in atherosclerotic aortas as compared with normal aortic intima-media. Although alterations in DNA methylation are well characterized in malignant tumors, the presence of methylation changes in atherosclerosis has not been studied even though both diseases are characterized by excess cellular proliferation and alterations in gene expression. Further anal. of the whole genomic methylation by high-pressure liq. chromatog. in normal and atherosclerotic aortas revealed a tendency for a decreased 5-methylcytosine (5-mC) content in atherosclerotic aortas as compared with normal arteries. Hypomethylation in atherosclerotic aortas occurred at the same level as has been reported from malignant tumors. Although a causal relation between the methylation level and expression of EC-SOD cannot be proven, the results show that ec-sod hypomethylation is assocd. with the development of atherosclerosis and suggest that it may affect structure and function of ec-sod and other genes possibly involved in the development of atherosclerotic lesions.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 11 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:2085 BIOSIS
DN PREV200000002085
TI Effects of secretable SOD delivered by genetically modified cells on xanthine/xanthine oxidase and paraquat-induced cytotoxicity in vitro.
AU Komada, Fusao [Reprint author]; Nishiguchi, Kohshi; Tanigawara, Yusuke; Iwakawa, Seigo; Okumura, Katsuhiko
CS Department of Hospital Pharmacy, School of Medicine, Kobe University, Kusunoki-cho, Chuo-ku, Kobe, 650-0017, Japan
SO Biological and Pharmaceutical Bulletin, (Aug., 1999) Vol. 22, No. 8, pp. 846-853. print.
ISSN: 0918-6158.

DT Article
LA English
ED Entered STN: 23 Dec 1999
Last Updated on STN: 31 Dec 2001
AB We designed a new eukaryotic expression vector for secretable superoxide dismutase (SOD), which expresses human SOD cDNA by fusing it to 1 connecting amino acid and the signal peptide DNA sequence of the human interleukin-2 (IL-2) gene (IL-SOD(2) cDNA). The ILSOD(2) cDNA constructed by PCR-based gene expression was ligated into the multicloning site of the pRc/CMV plasmid (pRc/CMV-ILSOD(2)). Rat lung epithelial-like cells (L2 cells) and rat skin fibroblasts (FR cells) were transfected with pRc/CMV-ILSOD(2) by lipofection. The extracellular SOD activities of IS(2)-L2 cells (L2 cells transfected with pRc/CMV-ILSOD(2)) and IS(2)-FR cells (FR cells transfected with pRc/CMV-ILSOD(2)) were 2-3 times higher than those of host cells. Initially, we investigated the protective effect of extracellular SOD secreted from these transformed cells (IS(2)-L2 and IS(2)-FR cells) on extracellular superoxide anion (xanthine/xanthine oxidase; X/XO treatment)-induced cytotoxicity in normal cells. The sensit ivities of these transformed cells to X/XO-induced cytotoxicity was decreased significantly as compared with that of host cells. Although, the conditioned medium from IS(2)-L2 and IS(2)-FR cells protected against X/XO-induced cytotoxicity, the conditioned medium from host cells (L2 and FR cells) showed no significant effects on X/XO-induced cytotoxicity. Furthermore, the conditioned medium from transformed cells was more effective than that of host cells against lipid peroxidation by normal cells under conditions of oxidative stress. Second, we generated superoxide anions in the intracellular space by paraquat treatment. The transformed cells were more sensitive to paraquat-induced cytotoxicity than host cells. Following addition of catalase, the sensitivity of these genetically modified cells to paraquat became equivalent to that of host cells. These results indicated a **protective** effect of transfection with secretable SOD genes against extracellular **superoxide anion**-induced cytotoxic ity although no such **protective** effect was observed against the intracellular cytotoxicity generated by paraquat treatment.

L7 ANSWER 6 OF 11 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1998:125273 BIOSIS
DN PREV199800125273
TI Cloning, characterization and overexpression of two iron superoxide dismutase cDNAs from Leishmania chagasi: Role in pathogenesis.
AU Paramchuk, Wendy J.; Ismail, Said O.; Bhatia, Ajay; Gedamu, Lashitew [Reprint author]
CS Dep. Biol. Sci., Univ. Calgary, Calgary, AB T2N 1N4, Canada
SO Molecular and Biochemical Parasitology, (Dec. 1, 1997) Vol. 90, No. 1, pp. 203-221. print.
CODEN: MBIPDP. ISSN: 0166-6851.
DT Article
LA English
ED Entered STN: 5 Mar 1998
Last Updated on STN: 6 Apr 1998
AB We have isolated and characterized two superoxide dismutase (SOD) cDNAs from a Leishmania chagasi promastigote cDNA library using degenerate primers derived from conserved amino acid residues of previously isolated manganese and iron SODs. Comparison of these two L. chagasi SOD deduced amino acid sequences with previously isolated MnSOD and FeSOD amino acid sequences revealed that they have higher homology to, and complete conservation of, invariant residues found in iron-containing SODs. Southern blot analysis showed that one gene, L.c.FeSODA, is a single copy gene, whereas the other gene, L.c.FeSODB, belongs to a multi-gene family. Transcript levels and enzyme activities of L.c.FeSODA and L.c.FeSODB show differential stage expression, with higher levels present in the amastigote stage of the parasite compared to the promastigote stage. Expression of the L.c.FeSODs in an E. coli SOD null strain

protected the bacteria against **free radical** generating agents. Overexpression of these FeSODs in L. chagasi parasites also showed enhanced **protection** against the **free radical** generating agents, paraquat and nitroprusside. The cloning, characterization and overexpression of the L.c.FeSODA and L.c.FeSODB genes and proteins demonstrates the possible role of SODs in Leishmania pathogenesis.

L7 ANSWER 7 OF 11 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 97:457076 SCISEARCH
GA The Genuine Article (R) Number: XC834
TI Use of the comet assay to investigate possible interactions of nitric oxide and reactive oxygen species in the induction of DNA damage and inhibition of function in an insulin-secreting cell line
AU Delaney C A; Green I C; Lowe J E; Cunningham J M; Butler A R; Renton L; DCosta I; Green M H L (Reprint)
CS UNIV SUSSEX, MRC, CELL MUTAT UNIT, BRIGHTON BN1 9RR, E SUSSEX, ENGLAND (Reprint); UNIV SUSSEX, MRC, CELL MUTAT UNIT, BRIGHTON BN1 9RR, E SUSSEX, ENGLAND; UNIV SUSSEX, SCH BIOL SCI, BIOCHEM LAB, BRIGHTON BN1 9QG, E SUSSEX, ENGLAND; UNIV ST ANDREWS, DEPT CHEM, ST ANDREWS KY16 9ST, FIFE, SCOTLAND
CYA ENGLAND; SCOTLAND
SO MUTATION RESEARCH-FUNDAMENTAL AND MOLECULAR MECHANISMS OF MUTAGENESIS, (29 APR 1997) Vol. 375, No. 2, pp. 137-146.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0027-5107.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 63
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB We have previously used the comet assay to demonstrate that the nitric oxide donor 3-morpholinosydnonimine (SIN-I) produces DNA damage in rat islets of Langerhans and in the SV40-transformed insulin-secreting hamster cell line, HIT-T15. Damage is not prevented by the addition of superoxide dismutase (SOD). In the present study, we have compared SIN-1, which generates nitric oxide, superoxide anion and hydrogen peroxide, with two other nitric oxide donors, S-nitrosoglutathione (GSNO) and the tetra-iron-sulphur cluster nitrosyl, Roussin's black salt (RES). We have used the comet assay as a highly sensitive method to measure DNA-damaging ability, and also measured inhibition of DNA synthesis and inhibition of insulin secretion. We have examined the effect of SOD and catalase on each of these endpoints in HIT-T15 cells following a 30-min exposure to the compounds (24 h for DNA synthesis), All compounds produced a significant dose-dependent increase in strand-breakage formation and all inhibited DNA synthesis and glucose-stimulated insulin secretion. RES was the most potent. SOD did not reduce the responses observed with any of the compounds. **Catalase** largely prevented **DNA** strand breakage, inhibition of DNA synthesis and inhibition of insulin secretion by SIN-1, but had no effect on responses to GSNO or RES. Addition of SOD together with catalase gave no greater **protection** against SIN-1 than catalase alone, The nitric oxide and **superoxide anion** produced by SIN-1 are thought to combine to form highly reactive peroxynitrite. In addition, H2O2 may be formed in the presence of SIN-1 and may form hydroxyl radical in the presence of a transition metal, such as Fe2+. It appears that in insulin-secreting cells, the effects of SIN-1 are largely mediated by this latter mechanism. In contrast, GSNO and RES appear to act by a different mechanism, not overtly involving reactive oxygen species. GSNO and H2O2 show no significant interaction in the induction of DNA strand breaks. Both nitric oxide and H2O2 are effective, directly or indirectly, as DNA strand-breaking agents, inhibitors of DNA synthesis and inhibitors of insulin secretion.

L7 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:600804 CAPLUS
DN 125:268872
TI DNA and RNA strand scission by copper, zinc and manganese superoxide dismutases
AU Dowjat, W. Karol; Kharatishvili, Malkhaz; Costa, Max
CS Nelson Institute of Environmental Medicine, New York University Medical Center, New York, NY, 10987, USA
SO BioMetals (1996), 9(4), 327-335
CODEN: BOMEEH; ISSN: 0966-0844
PB Rapid Science Publishers
DT Journal
LA English
AB Copper/zinc (Cu/ZnSOD) and manganese (MnSOD) superoxide dismutases which catalyze the dismutation of toxic **superoxide anion**, O2-, to O2 and H2O2, play a major role in **protecting** cells from toxicity of oxidative stress. However, cells overexpressing either form of the enzyme show signs of toxicity, suggesting that too much SOD may be injurious to the cell. To elucidate the possible mechanism of this cytotoxicity, the effect of SOD on DNA and RNA strand scission was studied. High purity prepns. of Cu/ZnSOD and MnSOD were tested in an in vitro assay in which DNA cleavage was measured by conversion of phage.vphi.X174 supercoiled double-stranded DNA to open circular and linear forms. Both types of SOD wee able to induce DNA strand scission generating single- and double-strand breaks in a process that required oxygen and the presence of fully active enzyme. The DNA strand scission could be prevented by specific anti-SOD antibodies added directly or used for immunodepletion of SOD. Requirement for oxygen and the effect of Fe(II) and Fe(III) ions suggest that cleavage of DNA may be in part mediated by hydroxyl radicals formed in Fenton-type reactions where enzyme-bound transition metals serve as a catalyst by first being reduced by superoxide and then oxidized by H2O2. Another mechanism was probably operative in this system, since in the presence of magnesium DNA cleavage by SOD was oxygen independent and not affected by sodium cyanide. It is postulated that SOD, by having a similar structure to the active center of zinc-contg. nucleases, is capable of exhibiting non-specific nuclease activity causing hydrolysis of the phosphodiester bonds of DNA and RNA. Both types of SOD were shown to effectively cleave RNA. These findings may help explain the origin of pathol. of certain hereditary diseases genetically linked to Cu/ZnSOD gene.

L7 ANSWER 9 OF 11 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 93:715859 SCISEARCH
GA The Genuine Article (R) Number: MJ387
TI EXPRESSION OF HUMAN CATALASE IN ACATALASEMIC MURINE SV-B(2) CELLS CONFERS PROTECTION FROM OXIDATIVE DAMAGE
AU LINDAUSHEPARD B A (Reprint); SHAFFER J B
CS NEW YORK STATE DEPT HLTH, WADSWORTH CTR LABS & RES, POB 509, ALBANY, NY, 12201 (Reprint); SUNY ALBANY, SCH PUBL HLTH, ALBANY, NY, 12222
CYA USA
SO FREE RADICAL BIOLOGY AND MEDICINE, (DEC 1993) Vol. 15, No. 6, pp. 581-588. ISSN: 0891-5849.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Reactive oxygen species have been implicated in aerobic organisms as causative agents in damage to **DNA**, proteins, and lipids. **Catalase** is a major enzyme in the defense against such oxidant damage. To determine whether increased catalase expression confers greater resistance to oxidant stress, a eukaryotic expression vector harboring a human catalase cDNA clone was constructed. Acatalasemic murine fibroblasts were then co-transfected with the catalase expression vector and pSV2-neo,

and successfully transfected cells were identified by their ability to grow in the presence of geneticin. Clones that contained integrated copies of the catalase expression vector were identified by Polymerase Chain Reaction (PCR) analysis. Stably transfected geneticin-resistant cell lines that overexpressed catalase in potentially positive cell lines were confirmed by catalase enzyme assays. To examine the physiological relevance of catalase overexpression, cells were exposed to oxidant stresses (hydrogen peroxide and hyperoxia), and survival rates were determined. Results demonstrated a significant resistance to oxidative stress in cells overexpressing catalase when compared to controls. These transfected cell lines will provide important models for further evaluation of the role of catalase in **protecting** cells against the toxic effects of oxygen-derived **free radicals** and their derivatives.

L7 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1990:34302 CAPLUS
DN 112:34302
TI Macrophage-mediated induction of DNA strand breaks in target tumor cells
AU Chong, Yen C.; Heppner, Gloria H.; Paul, Leslie A.; Fulton, Amy M.
CS Dep. Immunol., Michigan Cancer Found., Detroit, MI, 48201, USA
SO Cancer Research (1989), 49(23), 6652-7
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
AB It was shown previously that macrophages are mutagenic to bacteria and can induce the appearance of drug-resistant variants of murine mammary tumor cells. The present study asks whether inflammatory macrophages can induce lesions in the DNA of cocultured tumor cells and seeks to det. the mediators of this damage. The induction of DNA strand breaks was quantitated by using fluorometric anal. of DNA unwinding. The inflammatory macrophages coincubated with a mammary tumor cell line for 60 min at a 1:1 ratio result in significant nos. of strand breaks in the tumor cell DNA. The degree of damage is equiv. to 300-1200 rads of .gamma.-irradn. Resident (unstimulated) peritoneal macrophages also induce tumor cell DNA strand breaks. However, inhibitor studies reveal quant. and qual. differences in strand breaks induced by inflammatory (elicited) vs. resident peritoneal macrophages. Resident macrophages require a longer induction period (60 min) before breaks are detected, but induce more breaks than do elicited macrophages, which require only a 5-min coincubation period to induce damage. Catalase, which removes H2O2, protects tumor cells from both macrophage effector populations as does the prostaglandin synthase inhibitor, indomethacin. The **superoxide anion** scavenger, superoxide dismutase, and the lipoxygenase inhibitor, nordihydroguaiaretic acid, are **protective** only against resident macrophage effects. The metal chelator, o-phenanthroline, provides limited protection for elicited macrophages but induces total DNA breakage in the presence of resident macrophages. These data indicate that the degree of strand breakage is greater for the macrophage population with high arachidonate metab. and low oxidiatve metab. (resident macrophages) and less for the macrophage population with high oxidative and low arachidonate metab. (MVE-2 elicited macrophages). Both metabolites of reactive oxygen and arachidonate are implicated as mediators of this tumor cell DNA damage, with the relevant mediator dependent upon the particular macrophage population under study.

L7 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1984:546289 CAPLUS
DN 101:146289
TI Studies on the **protection** of DNA strand breakage induced by **free radicals**
AU Kim, Won Jin; Oh, Sang Hwan; Kim, Yoon Soo
CS Coll. Med., Yonsei Univ., Seoul, S. Korea
SO Yonse Uidae Nonmunjip (1984), 16(2), 373-86

CODEN: YUNMAV; ISSN: 0372-7858
DT Journal
LA Korean
AB An expt. was designed to investigate (1) if reactive O metabolites generated in in vitro systems influence DNA breakage, (2) if the destruction is by single radicals or 2 radicals cooperatively, and (3) to det. if **free radical** scavengers and detoxifying-enzyme systems function effectively in **protection** of DNA damage from these reactive O radicals. T4 phage DNA was not damaged by superoxide generated by the xanthine-xanthine oxidase system, and **superoxide dismutase** had no influence on the **DNA** damage. Neither 100 mM H2O2 nor Fe2+ plus superoxide produced by the xanthine-xanthine oxidase system caused efficient DNA damage. T4 phage DNA was not cleaved by reaction with superoxide and H2O2 (10 mM), but hydroxyl radical generated from 10 .mu.M Fe2+ and 1 mM H2O2 caused efficient DNA strand breakage, and the degree of strand breakage was proportional to the concn. of H2O2. About 50% of calf thymus DNA was cleaved by OH.bul. generated from the reaction of 10 .mu.M Fe2+ and 30 mM H2O2, and >80% of the DNA was cleaved by 10 .mu.M Fe2+ and 60 mM H2O2. The free radical scavengers mannitol and histidine both prevented T4 phage DNA damage from OH.bul. generated by the reaction of 10 .mu.M Fe2+ and 10 mM H2O2. The protective effect of 10 mM histidine against DNA damage by OH.bul. was similar to that of 50 mM mannitol. **Catalase** (0.5 units) protected T4 phage **DNA** from OH.bul. generated by 10 .mu.M Fe2+ and 10 mM H2O2, and glutathione peroxidase (0.67 .times. 10-3 units) protected DNA almost completely from damage under the same conditions. The protective effect of **glutathione peroxidase** against **DNA** damage induced by OH.bul. was .apprx.1000-fold stronger than that of catalase. The physiol. role of **catalase** and **glutathione peroxidase** in preventing the **DNA** damage by OH.bul. is significant, as the amt. of enzyme used in this expt. was much lower than cellular levels.

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